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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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EXAMINER	
KELLY, ROBERT M	
ART UNIT	PAPER NUMBER
1633	

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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/634,408	PARK ET AL.	
	Examiner	Art Unit	
	ROBERT M. KELLY	1633	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *10 March 2009*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1,4-8,18 and 21-33* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1,4-8,18 and 21-33* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Applicant's amendment and argument of 3/10/09 are entered.

Claims 1, 4, 8, 18, and 25 are amended.

Claims 26-33 are newly added.

Claims 1, 4-8, 18, and 21-33 are presently pending and considered.

Non-Finality of Office Action

It is noted that the Examiner did not address Claim 25 in the previous official action, and hence, the present action is non-final.

Claim Rejections - 35 USC § 112 - clarity

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 1, 4-8, 18, and 21-33 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 1 recites in the preamble "A method of reducing glomerulosclerosis", while the result of the method is delivery with an intent to reduce glomerulosclerosis, but does not require glomerulosclerosis is reduced. Hence, the Artisan could not determine if the claim is complete, or if other steps are required. Therefore, the claim is not clear for its metes and bounds.

Claim 8 recites the limitation "said population of human cells" in Claim 1. There is insufficient antecedent basis for this limitation in the claim.

Claim 8 also recites that the nucleic acid is transfected or infected into [the cell(s)], wherein [the cells are] delivered to the subject. The claim indicates that delivery is effected by transfection or infection. Such simply is incorrect and hence, lacks clarity for its metes and bounds.

Claim 18 recites in the preamble "A method of reducing progression of proteinuria", while the result of the method is delivery with an intent to reduce proteinuria, but does not require proteinuria is reduced. Hence, the Artisan could not determine if the claim is complete, or if other steps are required. Therefore, the claim is not clear for its metes and bounds.

Claim 25 recites in the preamble "A method of reducing progression of proteinuria", while the result of the method is delivery of the cells, but does not require the progression of proteinuria to be reduced. Hence, the Artisan could not determine if the claim is complete, or if other steps are required. Therefore, the claim is not clear for its metes and bounds.

Claims 4-8, 21-24 and 26-33 are rejected for depending at least one rejected base claim and failing to overcome the lack of clarity of the base claim(s).

Claim Rejections - 35 USC § 112 – New Matter

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 1, 4-7, 18, 21-24, 27, and 29-33 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement, for specifically embracing new matter. The claim(s) contains subject matter which was not described in the specification in such

a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

The rejected claims embrace the subject matter of administration of cells which naturally express IL-10 from an endogenous gene. Such is evidenced by dependent Claims 8, 26, and 28, when compared the language with that of the broad claims (e.g., Claim 1 or 18). In addition, the separately dependent claims also embrace such subject matter because they are separately dependent from the broad claims.

However, Applicant's original claims do not evince possession of such administrations of such cells to effect therapy. At best, the cells are transfected *in vitro* (e.g., Original Claim 8).

Moreover, the original specification teaches that (1) a gene is directly delivered and may be within a vector (e.g., paragraph 0012) and (2) the gene may transfected into a cell *in vitro* (e.g., paragraph 0013 and paragraph 0047). Further, the examples only demonstrate direct *in vivo* administration of the gene within a vector (e.g., EXAMPLE 4).

Hence, the original specification and original claims do not support the administration of cells which are not transfected *in vitro*. (Further, to make the language of record, it should be noted that the language newly added claim language to "transfected or infected" is not deemed to change anything, as the viral vectors would necessarily be infected, and the plasmids would be transfected. Still further, the language to *ex vivo* and *in vitro* with respect to these cells is considered the same, as they are both outside the body.)

Moreover, as these are amended claims, the specification and claims as originally filed must provide for possession of the invention as claimed, and hence, the Artisan does not have to look to the Art, as such would necessarily require obviousness to provide possession, and

possession is not demonstrated by obviousness, but by providing the blaze marks in the original filing to demonstrate possession of the invention.

Therefore, the Artisan would not have understood Applicant to have been in possession of cells which naturally express IL-10 for administration.

Response to Argument – New Matter

Applicant's argument of 3/10/09 has been fully considered but is not found persuasive.

Applicant argues that possession is provided by paragraphs 32 and 63 of the original filing (p. 5, paragraph 2).

Such is not persuasive. Paragraph 32 is drawn to humans and does not address the issue at hand. Paragraph 63 describes cell types which may be used but does not evince that it is meant to specifically encompass the use of naturally-IL-10-secreting cells.

Claim Rejections - 35 USC § 112 - enablement

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 1, 4-8, 18, 21-24, and 26-33 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention, for reasons of record.

Claim 25 is rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for Methods of treating glomerulosclerosis and progression of proteinurea in rodents, comprising delivery of a nucleic acid encoding IL-10 or allogeneic cells transformed to secrete IL-10, to the kidney, wherein cells of the kidney are transformed and secrete IL-10 in the case of nucleic acid transformations of kidney cells, thereby ameliorating autoimmune responses and ameliorating the progression of proteinuria or glomerulosclerosis, does not reasonably provide enablement for the lack of secretion of IL-10, species and *ex vivo* therapies with xenogenic cells. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention commensurate in scope with these claims.

Applicant's claims encompass treating any animal with kidneys (Claim 25), treating humans (all claims), ex vivo gene therapies with any cell type (Claim 25), and the non-secretion of IL-10 (all claims).

Such is broad the breadth of each of these genera, and the breadth of such is not such that the Artisan would reasonably predict that the various methods are efficacious for their breadth.

Treatment of Humans and any species of animal with kidneys

The core of the enablement is based upon the treatment of any species. As is of record, it was recognized at the time of invention that Applicant's experiments, carried out in rodent models, is not reasonably predictive of larger animals, including humans, which is taught in the specification (confluence of SPECIFICATION). To wit, as has been stated (e.g., Official Action of 11/21/05), Tomasoni, et al. (2004) Current Gene Therapy, 4: 115-22, provides a recent review of such therapies. First, Tomasoni recognizes the barriers which a vector must traverse to target

the specific tissues, which must be assessed in order to use them experimentally (p. 115, col. 1, paragraph 1), thereby recognizing the various aspects of gene therapy (vector targeting to deliver gene to enough cells and thereby express enough protein). Moreover, toxicity, immunogenicity, and efficiency are other aspects which may preclude any particular vector use (Id., paragraph 2). Further, each vector type contains various problems and advantages, and therefore, any particular vector is not reasonably predicted to produce enough of an effect for a long enough time. Lastly, Tomasoni concludes with a clear indication that gene therapy for renal disease (in humans) is a long way from being reasonably predictable. To wit, gene delivery is the major hurdle, and while looking feasible, studies are needed to establish if the present studies carried out in rodents will extrapolate to larger animals (p. 120, col. 2, paragraph 2). Moreover, identification of the causes of the various disorders are still required to identify the defective genes and be able to target them (Id.). Concluding, Tomasoni states "Much basic research is needed before gene transfer can be added to the therapeutic armamentarium for human kidney diseases." (Id.).

Hence, Tomasoni, writing an Artisan, recognizes that the rodent animal models, even when they are efficacious, require further testing in other animals to make the therapies reasonably predictable for humans. Moreover, Tomasoni recognizes that any particular gene delivery method encompassed will require confirmation to determine that enough cells are transformed, express and secrete enough protein, and do so for a long enough time to have a therapeutic effect.

Applicant's own post filing art, disclosing the same basic disclosure as the present Application, also echos the problems noted in Tomasoni (Choi, et al. (2003) Gene Therapy, 10: 559-68, p. 565, paragraph bridging columns), by stating that it would be useful to determine if

the same experiments can be extrapolated to other animals. Hence, it would appear that Applicant also recognizes the lack of reasonable predictability in the Art.

Secretion of IL-10

With regard to the secretion of IL-10, it is necessarily required to be secreted to act and have the effects, if not, it would just be a protein in a cell in the kidney, and not an anti-inflammatory agent. Hence, under this circumstance, the Artisan would not reasonably predict that an efficacious effect could be obtained as the IL-10 could not reach its target cell(s).

Xenogenic cells

With regard to the the breadth of cells which are modified and administered, it is well known in the Art that xenogenic cells would simply increase immune reactions, and simply therefore exacerbate the immunological responses which are the causes of the majority of disorders in the presently claimed embodiments.

Ex Vivo Gene Therapy

Also, for the record, with regard to the secretion of IL-10 from the cells to affect therapy, it is noted that there existed several methods to deliver cells to the kidneys, and because all that would be required is the secretion of IL-10 from these cells to have the same effect as a gene transfer method, it is difficult to argue that ex vivo approaches are not sufficiently enabled as far as delivering the IL-10 to the kidney, when the IL-10 is secreted (e.g., Kitamura (2000) Journal of the American Society of Nephrology, 11: S154-58, e.g., p. S154, paragraph 1); however, this alone is not sufficient to overcome the basic fact given above that the model used is not reasonably predicted to work for mammals other than rodents. (Applicant should note that this paragraph is not an attempt to argue that ex vivo therapy would work, as Applicant has appeared

to indicate in the argument of 8/5/08, but simply maintaining the logic of record with regard to delivery of cells expressing IL-10 as sufficiently enabled to provide IL-10 to the kidney, when the cells secrete IL-10, so that it need not be addressed again.)

Hence, the Artisan would have to experiment to determine if (1) these therapies would work in other animals than rodents, (2) whether xenogenic cells would not produced increased immune reactions which would exacerbate rather than ameliorate the problems, and (3) if non-secreted IL-10 would work, which amounts to inventing the breadth of Applicant's claimed subject matter for Applicant, and therefore, is considered undue.

Hence, Applicant's claims are considered to be non-enabled for their fully claimed scope.

Response to Argument - enablement

Applicant's argument of 3/10/09 has been fully considered but is not found persuasive.

Applicant argues that they have supplied a reference for consideration which demonstrates that the Artisan considered the FGS/Kist rodent model to be an art-accepted model for treatments of both glomerulosclerosis and proteinuria in humans (p. 6, last paragraph).

Such is not persuasive. Applicant has not supplied, nor even properly cited the article, and hence, no consideration is given. However, the aversion made by Applicant is that the Article states that the model is art accepted for both these therapies in humans, and given good-faith, the Examiner will for purposes of conjecture, discuss such. Park may indicate that the model is predictive of such therapies, but similarly, Tomasoni, cited above, was written the same year, and Applicant's own post-filing art (Choi, cited above) also do not reasonably predict it will work other animals, but suggest finding out whether or not it will work. Hence, it would appear that Park is not positive proof that the Artisan would consider the model to be reasonably

predictive the therapies at hand, but that Park considers it a model for such, while the Artisan is yet to decide. Further to emphasize the point, even Applicant says it would be useful to find out if it would work in other mammals, but does not state whether or not the model is "art accepted" for the therapies encompassed as a model for treating for any mammal and specifically humans. Hence, it would appear that Applicant scoured the Art to find someone who said something they wished to be said, rather than evidencing that the Artisan knew it to be predictive of such therapies as those claimed, for the breadth of any mammal or humans specifically.

Applicant argues that they are not required to cite art that is generally known or accepted by the Artisan (pp. 6-7, paragraph bridging).

Such is not persuasive. Given that the Art itself is unsure if it will work, while a sole article hypothetically says otherwise, it is clearly not generally known or accepted by the Artisan.

Applicant argues that Tomasoni report several successes, including allogenic cells (p. 7, last paragraph).

Such is not persuasive. Given that Tomasoni also reviews these successes, then argues that it is still a long way from being reasonably predictable in larger mammals and specifically humans, there is nothing inconsistent in the Examiner's rejection. This same reasoning has, and is still, part of the analysis provided by the Examiner (e.g., repeated ABOVE).

Applicant argues that the Examiner acknowledges "it is difficult to argue that *ex vivo* approaches are not sufficiently enabled" (p. 7, last paragraph).

As is addressed, it was clear from the rejection that *ex vivo* therapy is not what is enabled, but the actual delivery of cells and subsequent expression, and secretion of IL-10 to the target cells. Applicant is mischaracterizing the rejection previously provided.

Hence, the rejections remain, as modified by the amendments.

Conclusion

No claim is allowable.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to ROBERT M. KELLY whose telephone number is (571)272-0729. The examiner can normally be reached on M-F, 9:00am-5:00pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Joseph Woitach can be reached on (571) 272-0739. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Robert M Kelly/
Acting Examiner of Art Unit 1633